IN THE UNITED STATES DISTRICT COURT
FOR THE DISTRICT OF MASSACHUSETTS

IN RE:	)
	) No. 04-10981-PBS
NEURONTIN MARKETING, SALES PRACTICES, AND PRODUCTS LIABILITY LITIGATION	) MDL No. 1629)
This document relates to: KAISER FOUNDATION HEALTH PLAN, et al,	))
Plaintiffs	))
-V-	)No. 04-10739-PBS
	)Pages 1 - 95
PFIZER, INC., et al,	))
Defendants	)

JURY TRIAL - DAY SEVENTEEN

BEFORE THE HONORABLE PATTI B. SARIS
UNITED STATES DISTRICT JUDGE

United States District Court
1 Courthouse Way, Courtroom 19
Boston, Massachusetts
March 16, 2010, 8:54 a.m.

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I N D E X

P R O C E E D I N G S

THE COURT: Good morning. Good news, the juror is here, so ready to go. Robert gave her a rough thumbnail sketch about what we expected from her. She's fine with it. So we have the transcript, ideally speaking, and what I need is the -- do you have the chalks? Remember, she won't understand it otherwise, the little -- you may have forgotten that we needed to do Part B.

MR. SOBOL: We'll have them by 1:00. That's when she needs them.

THE COURT: Yes, and so I don't need to take her in right now, I don't think. I'll just have Mr. Alba give it to her, unless anyone has a problem with that, as soon as I've got a total packet.

Do we have the transcript? Oh, Lee remembers, so Lee has got the transcript, so --

MS. NUSSBAUM: We're redacting the transcript not to reflect the side bars and whatever?

THE COURT: Don't worry, she's got it.

So was there anything we needed to address about the trial today?

MR. SOBOL: One thing I was going to suggest, your Honor, is there might be a desire on the part of --

THE COURT: Don't stand up.

MR. SOBOL: Yes, thank you, and I'm going to be

leaving actually after the first witness too. I appreciate that.

The jurors might think, well, we should fill her in on what happened yesterday, so they should probably be told --

THE COURT: That's fine, I'll tell her what's going on.

Do we have anything about today's witness? Who is --

MR. GREENE: We have an issue with the slides, your Honor, that are going to be used with Dr. Brenner. I think we narrowed it down to one slide.

MR. HOOPER: It's actually a board, your Honor. Dr. Brenner relied on these systematic reviews we talked about. We have a board that breaks those out.

THE COURT: That's lovely, but not a soul in the world will be able to read it.

MR. HOOPER: The Cochrane one and the -- it's two reviews, so the point of the board is to say, here's what reviews are, and this is what they include.

THE COURT: What's the problem with that?

MR. GREENE: Well, he didn't review -- if you look at his report -- and we pointed this out to you in a motion in limine, your Honor -- he didn't review the negative studies. And the Cochrane -- can I finish?

THE COURT: No, no, no, no. No, he can't put in any opinion that he hasn't considered before. I was clear about

that with both sides. So he can't discuss anything that is not in his report.

MR. HOOPER: The reviews are in his report, your Honor, and the board shows what the reviews and what is in them, what they review.

MR. GREENE: Judge, the Cochrane review of 2005 didn't have POPP, didn't have Reckless. He's relied on a -- this is the subject matter of our motion.

THE COURT: Right, right. So I don't understand what you're -- is something on that chart that wasn't in the opinion?

MR. HOOPER: The two reviews are all cited right in his report, your Honor. And the pink shows that they're overarching, and then those are the studies cited in the reviews, what they review.

THE COURT: I'm not understanding the dispute.

MR. GREENE: Judge, putting the board up is implying that he reviewed all the studies. He didn't.

MR. HOOPER: I think he'll testify he did.

THE COURT: Are they in his report that he reviewed all those studies?

MR. HOOPER: The reviews are, your Honor. They're cited expressly, and the review --

MR. GREENE: The review is but not the studies.

THE COURT: No, then you can't put that up.

MR. HOOPER: Okay.

THE COURT: That's crazy. But let me just say this also. I hope this doesn't happen again. I was under the impression that there were just a few little objections to those depositions yesterday. It took me two hours yesterday. Everything was being objected to, and often I had to rule in subparts. So the big problem I found, I had a very difficult time getting through some of them. And when are they going to be played?

MR. CHEFFO: Today, your Honor.

THE COURT: So here's the issue: Some of them are clearly hearsay, clearly. Nevertheless, it is doctor-to-doctor communication, which is sometimes what doctors rely on, rather than necessarily the fraud, right? So that's their big cause thing. So that while some of it was hearsay, it may have been relevant if they said, like, "What did you hear, where did you hear it from? It might have been another psychiatrist who told me X." So when it looked to me as if that was maybe how one psychiatrist learned about a drug from another psychiatrist, I will allow it in for state of mind. Where it looked as if the statements went to whether it was efficacious or not, I excluded it, but the lines were often gray. And it was a lot yesterday afternoon, so I think I need to do, when these are being played, is say a lot of this is -- when I've allowed it in, and I don't even remember because I didn't keep a copy, is

that it's allowed in for state of mind only, not with respect to the efficacy of the drug. And so I think that's how I'm going to handle it.

MR. CHEFFO: I mean, to the extent that they're talking about other doctors and hearsay, I think, but if there is testimony that they did believe it was efficacious, that's not hearsay.

THE COURT: Well, let me put it this way: It's not hearsay. I don't think they're qualified on certain issues, but it's efficacious in their view based on their clinical, it's worked for them clinically, I've allowed in; not that it's effective in the way the FDA says it's effective. So I think I'm going to try and parse some of these lines before the depositions are played, which is, to the extent somebody says they relied on what another psychiatrist said, for example, it's not for the truth of the matters asserted; it's how he heard certain information, it's what his state of mind was when he prescribed. To the extent it's a doctor talking about, "Did you find it efficacious?" it's clinically efficacious; and if they're not relying on double-blinded studies, it's not scientifically effective.

MR. CHEFFO: Well, for our point, your Honor, I don't think that that would be an instruction to give to the jury at this point since, you know, we don't know in many of these cases what they're relying on.

THE COURT: Well, bingo, I agree. So these people are fact witnesses, not expert witnesses, and that's what I'm going to say to them. That's why I've allowed them in. It's over their objection. But I found it took me at least two hours. I thought there were lots of lines I was parsing. And you must have handed me eight depositions, some of which weren't so bad but for myself was brutal to get through.

MR. CHEFFO: That's the longest.

THE COURT: But it's also the most objected to by far, and I couldn't even tell with some of the snippets completely. So I'm at least confident of that one.

MR. CHEFFO: Your Honor, I know you want to bring the jury in. The only thing, and kind of in fairness, you didn't make any rulings on McCarberg, and, you know, we could have just played it; but I think, frankly, in fairness to them, you may not have gotten to this one, so we cut out a few things based on your prior rulings. I'd at least like you to take a look at what we cut out. You can look at their objections. So I didn't want to just play it without -- I don't know if you saw this.

THE COURT: Is it the same set of issues?

MR. CHEFFO: I think it's the same set of issues.

THE COURT: He's a regular doctor, one of the consumers?

MR. CHEFFO: And based on that, we cut out things

which I've highlighted which I thought you would cut out, and I just want to make sure we're all on the same page.

THE COURT: I'm sorry, I thought I got to everything. It took me forever yesterday.

MR. CHEFFO: And I appreciate you doing that on short notice.

THE COURT: But I am going to give those limiting instructions when I start: A, they're not Kaiser doctors; B, that sometimes it's hearsay, but it's for the state of mind of a doctor; and, C, these are not experts testifying to the scientific effectiveness, but they're talking about what happened to them clinically in their offices.

Is the jury all here, by the way? Do we know?

So as we're struggling through the instructions, unless plaintiffs give us authorities to the contrary, we're knocking out any jury instruction on unjust enrichment.

We believe, based on our research, that the Court decides interest.

We are still struggling through jury instructions for under the California unfair trade practices law. We might give you a draft on Friday, with you understanding that that piece of it is still rough.

We've got a draft jury verdict form that we're going to give you on Friday, and maybe even -- well, I'd like to actually see your opposition. I read last night the Motion For

Judgment as a Matter of Law. I'd like to probably read the opposition first, but right now, at least, I'm not even considering other states' laws.

And is there any other big -- oh, the measure of damages. Neither side really has submitted jury instructions on that, although it did come up in the Motion For Judgment as a Matter of Law, on whether I should just use the proximate causation standard or whether I should talk about the alternative theories and when you apply one versus another. Those are some big issues that I thought about on what to do with the jury. They've heard two separate measures of damages, so --

THE CLERK: All rise for the jury.

(Jury enters the courtroom.)

THE COURT: Welcome back. I hope you're feeling better.

Did anyone speak about the case or see anything in the press? I find the jury has complied.

Now, let me just say, what we decided to do, and just to put it right out there, is we're going to give you some -- remember, I'm not here tomorrow and the next day. I would say it's so you can celebrate St. Patrick's Day, but it's because I'm long ago committed to speaking at a sentencing seminar in New Orleans, so I'm flying down tomorrow afternoon and back Thursday afternoon. So in those two days, I've got reading

materials for you. Lee has prepared a transcript and the little chalks that go with them for you to read, and then you'll give them back on Friday, okay, so you'll get caught up. We're starting with a brand-new witness today, so it will be pretty easy for you to segue into today's, and then you can just read it. You know, don't read it right before you go to bed.

(Laughter.)

THE COURT: All right, so I think that's how we'll handle it. She'll get caught up. I really appreciate everybody here is cooperating. We really wanted to keep you on the jury, and I appreciate your coming right back in. I understand everyone in your family is sick, so just don't give it to us.

(Laughter.)

THE COURT: So we're going to get going on our next witness.

MR. HOOPER: Thank you, your Honor. We call Dr. Gary Brenner.

GARY J. BRENNER, M.D.

having been first duly sworn, was examined and testified as follows:

THE CLERK: Will you please state your name and spell it for the record.

THE WITNESS: Gary J. Brenner. That's G-a-r-y J.

B-r-e-n-n-e-r.

DIRECT EXAMINATION BY MR. HOOPER:

Q. Good morning, Dr. Brenner.

A. Good morning.

Q. What is your profession?

A. I'm trained as a physician and basic science researcher, and I practice pain medicine basically full time.

Q. And where are you employed, sir?

A. Massachusetts General Hospital.

Q. Could you please describe first your educational background.

A. Certainly. I did my graduate training at the University of Rochester. I earned a medical degree, and I also did a Ph.D. in immunology and neuroscience.

Q. Could you please tell us about your medical training after you got your Ph.D. and your medical degree.

A. Sure. After Rochester, I came to Boston to train at Mass. General, first, in a full residency in anesthesiology, which is three years plus some internal medicine training for a year, and following that, I did some additional training, which is a year fellowship in pain medicine, also at Mass. General.

Q. Are you board-certified in any specialty, sir?

A. I'm board-certified in both anesthesiology and pain medicine. Those are separate boards.

Q. Dr. Brenner, what are your current professional

responsibilities?

A. Well, I'm an assistant professor of anesthesia at Harvard Med School, and I teach residents, fellows, pain medicine fellows, and also some memorandum students. And I attend, which means I have a medical practice, at Massachusetts General Hospital, and at this point that's a hundred percent pain medicine two days a week. And also I'm federally funded to do research in the basic science of pain, what causes pain hypersensitivity and chronic pain.

So just to break it down, I'd say I'm 40 percent clinical work, seeing patients, 40 percent doing research, and 20 percent is administration because I'm also the director of the Mass. General pain medicine training program.

Q. Doctor, have you published in any peer-reviewed journals on the mechanism of pain?

A. Absolutely.

Q. And have you published any book chapters in textbooks about how the mechanisms of pain relate to treating patients?

A. Yes. I just recently published in one of the two preeminent textbooks in anesthesia, the chapter on pain mechanism.

THE COURT: We've learned a lot about this. Is this neuropathic pain or nociceptive pain?

THE WITNESS: Well, that's an interesting question. The focus of my research is really on the mechanisms that cause

hypersensitivity. So how does a normal nervous system, where when you stub your toe it hurts and then it stops hurting, get to a point where you have pain all the time and pain without stubbing your toe and also pain to things like light touch? So trying to understand the mechanisms that turn the normal nervous system into a pathological system where you have neuropathic pain because neuropathic pain is by definition pathology.

Q. Dr. Brenner, I want to turn to the subjects you focused on in this case, but let me ask you first, you're not a doctor who has marketing training or experience?

A. No.

Q. We didn't ask you to look at any marketing documents in this case or offer any marketing opinions?

A. You didn't ask me to offer any marketing opinions, but I have read many of the plaintiffs' expert reports, and they certainly do comment extensively on marketing. So I have seen documents vis-a-vis the expert reports.

Q. Other than that, you're not a marketing expert?

A. Not at all.

Q. And as I understand it, are you a biostatistician by trade?

A. No. I have training in statistics through both my medical training and through my basic science training and use it on a daily basis. So what I'd phrase this as is, I certainly do

have expertise in the area, but certainly not nearly as much as many other people.

Q. And in the area of clinical trial design and study methods, is that something that you're an expert in?

A. I would give you the same answer. That's not my expertise. I have the level of expertise that you'd expect of anyone who went through medical training. And as a side point, for several years I've been working on the -- it's Partners, which is Mass. General and the Brigham and some other hospitals, their institutional review board. So as a member of that, I review ongoing clinical trials for Partners to make sure they're conducted properly and safely. So I have some experience through that, but, again, there are many people with more expertise.

THE COURT: So would you call yourself an expert in clinical trials?

THE WITNESS: I would say I have experience, but I wouldn't call myself a true expert in terms of that small proportion of people who really understand the field better than virtually everybody else.

Is that clear enough, your Honor?

THE COURT: Well, let me just ask you, are you holding yourself out today as an expert in clinical trials or an expert in pain?

THE WITNESS: I'm definitely an expert in pain

medicine. Clinical trials, I'd probably say "no."

Q. Doctor, let me ask you, what did you focus on in this case?

A. The efficacy and the utility of gabapentin for the treatment of patients globally, and also my personal practice, the patients I treat at Mass. General, almost always with trainees, usually pain medicine fellows.

Q. And did we also ask you to be prepared to explain the different pain categories, some of which Judge Saris just mentioned?

A. Certainly, and that really is -- I would say that I'm a true expert in any sense of the word on types and mechanisms and treatment of pain clinically, and the basic science too.

Q. And did we also ask you to look at medical decision-making process?

A. Yes.

Q. Okay.

A. Which is part and parcel of treating patients with pain, of course.

Q. And there were certain Kaiser claims relevant to your expertise that we asked you to look at as well?

A. Correct.

Q. Doctor, can you briefly describe the kinds of materials you reviewed in connection with your work in this case.

A. Sure. I did my own literature review of the current state

of understanding of efficacy of gabapentin for a variety of types of pain; and I reviewed a wide variety of expert reports, first, from the plaintiffs actually because I thought that was more important for me to see the other side's point of view, and then more recently from the defense. And, of course, as part of this whole process for me is my experience and expertise. I've been practicing pain medicine for at least ten years, no matter how you want to slice it, and I have been board-certified in the area since 2002 -- 2001, I think -- I get a little mixed up -- and have been running the Mass. General training program in pain medicine since 2002. So I can't divorce my professional experience from my opinions.

Q. Are you generally aware of the criticisms that Kaiser's experts have with studies like the Backonja, the Gorson, and the Reckless study?

A. Yes. And I would add that in the materials that I reviewed, both by the plaintiffs and the defense, there's a great deal of discussion of those trials.

Q. Doctor, did you also look at something called Expert Consensus Guidelines in connection with your work in the case?

A. I did.

Q. And what are Expert Consensus Guidelines?

A. Well, there are groups of individuals who should have and do have expertise in the particular area they're opining upon or giving an opinion on, and basically they get together and

look at the global literature, what's there, what's not there, and come up with some guidelines to help physicians approach patients with a given problem. Of course, in this case I was looking at consensus opinions related to pain management, particularly neuropathic pain management.

Q. And another thing that you looked at was something called "systematic reviews"?

A. Yes, systematic reviews and meta-analysis, of course.

Q. As a practicing physician, why are systematic reviews and Expert Consensus Guidelines something that you would look to for information?

A. Well, I think everyone realizes that we're bombarded with information these days, and medicine and science is no different. And there are literally, just talking about Neurontin, there are thousands of papers related to Neurontin. And I think that consensus statements by experts and meta-analyses performed by people with the appropriate expertise, those kind of approaches are essential to allow physicians who are very busy, bombarded by a lot of information, some of which may be not that relevant, to really help them grasp what's known and to optimally treat their patients. That's the bottom line. These kind of approaches help individual physicians optimally treat individual patients.

Q. Doctor, before we get into the details, could you give the jury a brief summary of your opinions in the case.

A. Sure, and as of today, and I stand by this -- I know I wrote this report some time ago, but my opinions haven't changed in any way -- I do believe, based on the types of data we discussed recently, that gabapentin is substantially helpful for patients with neuropathic pain. And that's not to say every patient, but it's very helpful for a subset of patients with neuropathic pain. And this is not something that is important to my practice, but there's certainly good evidence from the medical literature that even a single dose of Neurontin before an operation can decrease pain and decrease, like, morphine use after an operation. And I think that's very interesting because it tells me, you know, there's something there in terms of its mechanism of action that really requires further study, but just so you know, I'm not -- perioperative pain management, though, I do practice it, is not a major focus of what I do.

Q. And how about safety, what are your opinions there?

A. Sure. Gabapentin, it's just a fact, it's probably, of the major medications we use for treating neuropathic pain, it's as safe as any of them. It has a similar safety and efficacy profile to pregabalin because they're very similar medications -- it's also known as Lyrica -- but it certainly compares favorably and better than most of the others.

Q. And with reference to the last bullet on the slide, what's your opinion as to gabapentin's place as a therapeutic option

in treating neuropathic pain patients?
A. Certainly. What I would say is -- and, again, this is very clear in my report -- we don't have magic bullets for treating neuropathic pain, and none of the medications or treatments we have work on all patients. What I would say about Neurontin is, for, again, and I mention this, for a subset of patients it's extremely effective; and if we didn't have access to this medication, for several reasons, we'd really be substantially limited in our ability to treat certain patients.
Q. Dr. Brenner, I want to turn now to the clinical experience you told us about. How many patients are you treating for neuropathic or chronic pain in total right now, best estimate?
A. My best estimate would be somewhere around 175, give or take 200, for neuropathic pain; and then obviously my global patient population is much larger, but not all of them have neuropathic pain.
Q. And are most of the neuropathic pain patients that you see referred to you by another doctor?
A. In some senses, they're all referred to me by another doctor because you can't get into a subspecialty clinic without a referral. But to be really clear, like, some of my patients are very happy with the care they've received -- well, I hope mostly almost all of them are -- but happy enough that they'll refer friends to me. So in that sense, it's a little

different. It's almost like either -- sometimes I get patients also through social friends who know I practice pain medicine. You got the picture.

Q. Sure, sure.

MR. GREENE: Objection, your Honor. Motion to strike.

THE COURT: Overruled.

MR. GREENE: Clinical experience, and we have no patient reports.

THE COURT: Overruled. How he was referred patients?

Q. Your patients that come to you who are referred to you by other doctors, those are, to put it in the common parlance, they're patients who were sent to see a specialist, and you're the specialist? Is that the way it works?

A. Yes, correct.

Q. And do your patients have a variety of different pain conditions?

A. Absolutely, a wide range, and I'd broadly group it, they're almost all chronic pain patients. There's neuropathic pain patients, patients with cancer pain, patients with chronic pain due to rheumatological like arthritic conditions. And then we do happen to see a subset of patients who their primary problem is dependence on opioids or narcotic dependence and abuse. They may or may not also have a pain problem, but as a pain medicine expert, I have real understanding of how morphine-like drugs should be used and how they're abused, and

I often am referred patients to try to help with that problem.
Q. And for the variety of pain conditions that you see, do you prescribe a variety of different kinds of treatments?
A. Absolutely.
Q. And do you prescribe Neurontin for some of your pain patients?
A. Absolutely.
Q. Do you use Neurontin both on-label for postherpetic neuralgia and off-label for other kinds of pain conditions?
A. Yes.
Q. Are you familiar with the prescribing practices of some of your colleagues who you train and work alongside at Harvard and Mass. General?
MR. GREENE: Objection, your Honor.
THE COURT: I'll just allow yes or no.
A. Yes.
Q. Do they prescribe Neurontin for neuropathic pain?
MR. GREENE: Objection.
THE COURT: Sustained. Hearsay.
Q. Can you give us an idea of the kinds of pain problems for which you use Neurontin in your own patients?
A. Sure. In my practice, and this is what I teach my fellows is, I limit my use of Neurontin mostly to, and leaving perioperative pain out of this, but in terms of the clinic population, for patients who have at least a component of

neuropathic pain. And what's complicated about this is, patients don't fit into little peg holes. You know, many patients have multiple different problems and multiple different types of pain. So if we feel that there's at least a component of neuropathic pain, it's certainly a medication that would be considered.

Q. Are there any institutional or insurance-coverage-related restrictions on your ability to prescribe Neurontin for pain patients, formulary status, guidelines, anything like that in your case?

MR. GREENE: Objection, your Honor.

THE COURT: Is it in his -- is it beyond the scope of his opinion?

MR. GREENE: No, it's not in the report.

THE COURT: Sustained.

Q. Doctor, about how many of your current pain patients are you treating with Neurontin?

A. My best estimate would be roughly 20 percent of my patients who have some form of neuropathic pain or a component.

Q. And how many different --

THE COURT: So in absolute numbers right now, how many people would you say are in that category?

THE WITNESS: Well, if I were just to say roughly 200 patients and 20 percent, then I would estimate 40 patients currently.

Q. And of the remainder --

THE COURT: And how many of those are for postherpetic as opposed to something else?

THE WITNESS: I don't have a large population of postherpetic neuralgia, so I have -- right now I'm actively following three patients with postherpetic neuralgia, and the best of my recollection, they're all on gabapentin, each of them.

Q. So about 37 of the 40 would be being treated with gabapentin for something other than postherpetic neuralgia?

A. That's correct.

Q. Doctor, are you treating any patients who were referred to you after having tried medications other than Neurontin or gabapentin without success?

A. Certainly. In fact, almost virtually all of my patients have been treated --

MR. GREENE: Objection, your Honor. Motion to strike.

THE COURT: Yes.

Q. Doctor, have you treated any patients who had failed on other medications, started on --

THE COURT: Can I see you at side bar just for one second.

SIDE-BAR CONFERENCE:

THE COURT: I just want to remind you just so I don't get into this, there was a discovery order early on that you

couldn't get into individual patients unless you produced the documents of those patients. And so while I've allowed you to talk about his general clinical experience, you can't get into individual patients and their success or lack of, and I don't know what documents you've produced or not produced, but --

MR. RONA: Haven't produced anything.

THE COURT: So while I don't have a problem with his general experience -- he obviously is quite knowledgeable in that -- just I won't know where you're going. And I don't really know the report that well as to, or the deposition, as to what he's already disclosed in the report and deposition.

And I don't know when you jump up unless you say something like "beyond the report," I won't know what the basis is.

MR. GREENE: Well, I tried to alert you earlier that they haven't produced any patient records, and he's talking about now clinical experience.

THE COURT: That's why I brought you to side bar, yes. No, I allowed him to talk in general he's found efficacious; but as soon as you get into, "And I have these three patients who had X," you had to have produced the reports. So just before we got into it --

MR. HOOPER: Can I tell him not to do that so that he doesn't blurt it out accidentally?

THE COURT: Well, I can do it.

MR. SOBOL: He should have been told beforehand.

MS. NUSSBAUM: Let the Judge do that.

MR. CHEFFO: Why don't you say in general, just ask some general questions about his practice that don't get into the specifics.

MR. HOOPER: I'm not asking him about individual patients.

THE COURT: I didn't know where you were going, that's all.

(End of side-bar conference.)

THE COURT: So what were we chattering about over there? You might all be interested. As you know, before this case, there was a lengthy period of pretrial discovery, and one of the lines that we drew is that you wouldn't be talking about individual patients unless you had produced their medical records. So while I'm allowing you to talk about your general clinical experience, I'm not going to allow him to go into, "This patient, this happened, and this patient, that happened," simply because we don't have those medical records in front of us. And part of that had to do with privacy concerns, and part of that had to do with just the volume of materials that might have to come in.

So when you're talking based on your clinical experience, you can give us certain opinions about the clinical experiences you've had but not this patient X and Patient Y.

Okay? So that's what we had worked out as a road map before this trial began.

BY MR. HOOPER:

Q. Doctor, in reference to your overall clinical experience and without reference to any specific patients, has it been your experience that Neurontin sometimes is effective where other medications have failed?

A. Absolutely.

Q. And, Doctor, based on your overall clinical experience, do you believe Neurontin is an effective pain medication for your patients?

MR. GREENE: Objection, your Honor.

THE COURT: I'll allow it based on his clinical experience.

Q. Without reference to individual patients.

A. Yes, and I'll answer that question exactly as I've said today already, which is, for a subset of patients, it's very helpful for them. It's effective, improves their pain, and can help improve functional status and quality of life, so, yes. And I will, because I really just want the jury to understand --

MR. GREENE: Well, objection, your Honor.

THE COURT: Yes, sustained.

MR. GREENE: I think he's answered.

THE WITNESS: Okay, sorry, your Honor.

Q. Doctor, let's start with some basic terminology. First, what is nociceptive pain?

A. Nociceptive pain is the pain that occurs with a healthy normal individual when some sort of noxious stimulus -- and that can be physical like stubbing your toe, temperature like extreme heat of a fire or extreme cold, or a chemical stimulus -- comes close enough to the body to activate the pain system. And it's basically the body's alarm system that there's danger in the environment. If you get away from that stimulus fast enough, such as the heat of a stove, there may be no injury. If you don't withdraw, then there could be subsequent injury. But if you get away from the stimulus fast enough, then when you get away from the stimulus, in very short order the pain goes away.

Q. When you break your leg, would that be nociceptive pain?

A. There would be a component of nociceptive pain when you break your leg, but of course there's injury. So anytime there's injury, there's also going to be the development of inflammation as part of the healing process, and that will cause inflammatory pain. So I think one thing that you're going to learn is that people don't get boxed into one type of pain alone, that they're overlapping, and you can have more than one.

Q. In your work in this case, did you learn that Kaiser claims in part that some of its doctors prescribed Neurontin

for nociceptive pain?

A. I did.

Q. And what was your reaction to learning that?

A. My reaction was, frankly, I've never heard of -- I have never prescribed gabapentin for nociceptive pain such as also like a dental procedure, for example, or a broken arm, and I've never actually heard of anyone in all my work teaching and lecturing of anyone who had. So I was a little confused, in that it's just not something I'd ever think of.

Q. What is inflammatory pain briefly?

A. Inflammatory pain is pain of the nervous system associated with inflammation. Inflammation can occur two ways: One is anytime, as I said, you have an injury, the healing process involves inflammation. There's also some diseases such as arthritis which have chronic inflammation.

Now, there is a difference between the nociceptive and inflammatory because one thing that's true of inflammatory pain and neuropathic pain, as I'll mention in a second, is that basically you turn the gain up on the pain system. So three things happen: One is, sensation that normally wouldn't be painful becomes painful. So like after you get a sunburn, that's inflammatory pain. Stroking of the skin which normally feels good becomes painful, or a warm shower that might feel good becomes painful. Secondly, something that would normally be painful like a hit becomes more painful. So nonpainful

becomes painful, painful becomes more painful. And the third thing I'm going to tell you about is, you can have pain without any stimulation. That's called spontaneous pain.

The inflammatory pain, unless it's a chronic disease, like nociceptive pain, is physiologic or helpful for the body because what it does is, that injured area becomes sensitive or sensitized, and that helps prevent that area from getting further injury while healing occurs. And with inflammatory pain, once healing occurs, that increased gain or sensitization goes away. So it's helpful for the body. It's physiologic, we say.

Q. And what's neuropathic pain?

A. So neuropathic pain occurs with injury or dysfunction for a variety of reasons of the nervous system. And it has a lot of those similar clinical findings as inflammatory pain. So sensitivity to nonpainful stimuli, increased pain with something that's already painful, and spontaneous pain. The difference is, it more often than not doesn't resolve on its own; and, secondly, unlike nociceptive and inflammatory pain, there's no known benefit to the body, to the organism, to the person. So we consider that a pathology. Just like heart disease, bad heart disease doesn't help the individual in any way, neuropathic pain also doesn't provide any benefit to an individual.

Q. Doctor, what are some of the different types of pain

conditions that you would classify as neuropathic pain?
A. So I'm sure everyone has heard about postherpetic neuralgia and painful diabetic neuropathy. Those are two typical types of neuropathic pain that are used for clinical trials and clinical studies, partially because a lot of people have it so it's easy to find the people to study, but there are many, many other forms of neuropathic pain. Those both involve injury to the peripheral nerves, so the nerves outside of the spinal cord and brain, but spinal cord injury can cause neuropathic pain. Strokes, for example, an area called the thalamus or thalamic strokes, well known to cause neuropathic pain.

But there are many, many other causes; chemotherapeutic agents, several of which can damage the nervous system and cause neuropathic pain. Cancer, when that tumor invades a tissue and presses on a nerve, can cause neuropathic pain. Many operations -- and this isn't well known -- have a very high incidence of neuropathic pain. So, an example, inguinal hernia repair, depending on the study you look at, it might be as much as 50 percent of individuals will have significant neuropathic pain. So there are actually many, many causes.
Q. Doctor, in your report you discuss something called "perioperative pain." What is perioperative pain?
A. So perioperative pain is really the pain that surrounds an operation, and usually we think the first one or two weeks. If

it's much longer than that, it's not really perioperative. And it includes a couple different components or types of pain. One is the nociceptive pain because virtually all operations involve mechanical injury. And then there's inflammatory pain because there's healing after the operation causing inflammation and inflammatory pain. And, as I just mentioned, a variety of operations are known to cause neuropathic pain. And I would just say, I want to add so this is understood that inflammatory pain that has that sensitization and neuropathic pain that also has sensitization, though in many ways they're fundamentally different, they are thought to share some similar underlying mechanisms.

Q. Is there evidence in the medical literature that you reviewed to support the use of Neurontin in perioperative pain in some patients?

A. There's evidence, as I mentioned, that gabapentin, even a single dose before an operation, can decrease pain and decrease narcotic or morphine consumption after an operation, which is often used as a surrogate measure of decreased pain.

Q. And what is acute pain, acute?

A. Acute pain is thought to be kind of the immediate pain that occurs after an injury like a broken bone. We usually think it should resolve in the first -- you know, this is very arbitrary, but people say three months just as an arbitrary time frame.

Q. And what is chronic pain?
A. Chronic pain is the pain that persists beyond three months. Some authors might say six months. Again, it's somewhat arbitrary. It's just to distinguish the two.
Q. Let's turn to your opinions on effectiveness. First, to your knowledge, has Neurontin been approved for a broad neuropathic pain indication in other countries that have pharmaceutical regulatory agencies?
A. It has.
MR. GREENE: Objection, your Honor.
THE COURT: Overruled.
MR. GREENE: Move to strike the answer.
THE COURT: Overruled.
A. In particular, in European countries that have --
MR. GREENE: Your Honor, this is beyond the scope of his report.
THE COURT: Oh, sustained.
MR. HOOPER: Your Honor it's in his report. I can show you.
THE COURT: Show it to him then.
MR. GREENE: Could we have a side bar?
THE COURT: Just to explain, the basic rules are, they give an expert report beforehand, and they're pretty much limited to that so the opposing side isn't surprised at all. So you'll hear these disputes sometimes about what was or

wasn't in the report.

Q. Doctor, I'll ask you again. To your knowledge, has gabapentin been approved for the treatment of neuropathic pain in more than fifty countries?

A. That's my understanding, including some European countries --

MR. GREENE: Objection, your Honor. He answered the question.

THE COURT: I'll allow that.

Let me just say this: With respect to other countries, we have our own set of standards in this country that are not necessarily the standards in other countries. So I've allowed in this evidence because it may be what doctors are hearing about, but it does not control what is efficacy under the FDA standards. So that's --

Q. Doctor, is there any medication that is approved in this country by the FDA for use in treatment of neuropathic pain in the broad sense, meaning any and all kinds of neuropathic pain?

A. No.

Q. And given that FDA hasn't approved any medications for neuropathic pain in this broad sense, is there an FDA-approved medication for each of those separate neuropathic pain conditions that you told us about that you treat?

A. Absolutely not.

THE COURT: Well, there is for some of them, right?

THE WITNESS: But not -- oh, sorry, your Honor. I understood the question as, is there something for everything? So there certainly is -- there are drugs approved for PHN, postherpetic neuralgia.

THE COURT: That's shingles, right?

THE WITNESS: That's a sequelae to shingles that occurs in about 10 percent of people. There's medications FDA approved for painful diabetic peripheral neuropathy. There's approval for -- and this is a little more murkier -- fibromyalgia. Whether or not that's neuropathic pain there is debate about.

THE COURT: So as I understand it, the FDA has taken the approach of looking at, what would you call them, subsets of neuropathic pain?

THE WITNESS: I think that's a reasonable way to describe it.

Q. Doctor, you mentioned in your report that Neurontin is approved for postherpetic neuralgia, and we've heard lots about that. Why is that significant to you?

A. Postherpetic neuralgia is unquestionably a form of neuropathic pain. It probably actually has two different -- there's probably two different types of postherpetic neuralgia based on the underlying mechanism. So it's important to know that there's strong evidence that the FDA accepts that gabapentin or Neurontin treats what I'd really call two forms

of neuropathic pain in this case; and that tells us that as a practicing pain medicine doctor, it's something I want to think about for treating patients with other forms of neuropathic pain.

Q. Doctor, are any of the tricyclic antidepressants or TCAs approved by FDA for any kind of neuropathic pain?

A. They're not approved for any form of pain, period.

Q. Doctor, I want to turn to the literature that you cited in your report, particularly the two systematic reviews, Cochrane and Millegars.

MR. GREENE: We have a question, your Honor.

THE COURT: Oh, yes, go ahead.

A JUROR: Not to get too far into the weeds, but are the mechanisms for PHN and PDN and all these other things, are the mechanisms of cause the same?

THE WITNESS: I think that's an excellent question, and in fact every expert in the field of the underlying mechanisms asks exactly that question, and it's very complex. I'd say there are multiple mechanisms that cause neuropathic pain. And it's actually even more complex than that because for a given individual with neuropathic pain, there's almost no question that the mechanisms that are causing the neuropathic pain in that individual change over time during the course of their disease, their illness with neuropathic pain. So the way we're really thinking of this is different forms of neuropathic

pain, and really all that matters is the one individual in terms of treatment, right? Because we don't treat populations; we treat one individual. So the belief in the field now is that you can have two people with completely different mechanisms that, again, are changing over time, and you can also have two people with different forms of neuropathic pain that share some mechanisms but also have unique mechanisms, and you can also extrapolate that to different disease states in general. Does that make sense?

And I would add that --

THE COURT: Well --

THE WITNESS: Well, we do understand a lot of the underlying mechanisms through basic science research.

THE COURT: We'd better not go into all of them because it's beyond the report, and I think we should probably stop it there.

THE WITNESS: Okay. I just want to say that's really a fantastic question.

A JUROR: Really just have to pick things up.

THE WITNESS: Okay.

MR. HOOPER: All right, your Honor, I want to move Exhibit 1772 and 1478, which are a Cochrane review entitled "Gabapentin and Acute Chronic Pain" and a second one by Mellegars, "Gabapentin for Neuropathic Pain --"

THE COURT: Isn't Cochrane in? No?

THE CLERK: 1772 is in and 1478 is not.

(Exhibit 1478 received in evidence.)

Q. Doctor, these are two systematic review articles that you cited in your report, correct?

A. Yes.

Q. First, can you briefly explain what systematic reviews are and why you think they're important.

A. Well, as I said earlier, they're reviews that look at either the whole literature or subsets of the literature. They come in different forms; for example, meta-analyses, which tend to be more restrictive in terms of what they will accept in terms of data analysis. That's because there is a clear protocol in performing them versus a more global systematic review that might be much less restrictive in terms of what components of the medical literature they'll look at. And to be specific, the meta-analyses tend to restrict themselves more to the double-blind placebo-controlled trials, though not always; and the systematic reviews may be willing to look at other forms of evidence like the open trials where people know what medications they're receiving.

Q. And do I understand correctly that the reviews will take double-blind studies, for example, and look at a whole bunch of them together and come to conclusions about all of the studies?

A. That's correct.

Q. Could you turn to Page 6 of the Cochrane one, 1772. And

do you see the part where it says "References to studies included in this review"?

A. Yes.

Q. The first one listed there is Backonja, and that was in painful diabetic neuropathy; is that right?

A. Correct. That's the JAMA publication.

Q. And next is a study by -- a study included in the Cochrane is the study by Bone in 2002; is that right?

A. Correct. That was on post-amputation phantom pain, which is a form of neuropathic pain.

Q. What is post-amputation phantom limb pain?

A. So after people lose a finger, a limb, or it can be virtually any part of the body, almost every person actually will have sensations that appear to be in that part of the body that's lost. A smaller percentage of people will develop persistent -- it can be really agonizing -- pain that seems to occur in that part of the body that's lost, and the typical thing people always think of is like a leg or an arm.

Q. And the next study there listed is a study by Caraceni and colleagues from 2004. Do you see that one?

A. Yes.

Q. What form of neuropathic pain was that in?

A. Neuropathic pain associated with cancer.

Q. And the next one at the top of the column is Dellochio 2000. What type of pain was studied there, and what was the

control.

A. So that was an active control study, which can be blinded but it's not placebo-controlled. And these are important studies. Instead of comparing your drug to placebo, you compare it to a drug for which there is already evidence that it's helpful in that condition. And that was looking at painful diabetic neuropathy, and they compared it to a tricyclic.

Q. The next study listed there is by Dirks 2002, and what condition did they study there?

A. Postoperative or perioperative pain. They're basically the same thing.

Q. The next study below that is Gorson, and that was diabetic neuropathy?

A. Correct.

Q. And next below that is Morello 1999. That was also a diabetic neuropathy study?

A. Correct, also an active control, a tricyclic.

Q. Okay. And the next one will throw us all because this is Pandey but not the same Pande. This is Pandey with a Y at the end. And what kind of pain did the Pandey with the Y study involve?

A. Neuropathic pain. It's called Giambre syndrome, which is thought to be caused by a viral illness, so that's another form of neuropathic pain, which is response in infection.

Q. And if you could look going at the references as they go onto the next page, we're almost finish, but at the top there's a study by Perez 2000 included in the Cochrane review. What type of pain was that?

A. Diabetic neuropathy.

Q. And the Rice 2001 study below that, what type of pain did they study?

A. That was PHN.

Q. And Rowbotham, 1998, also PHN?

A. Yes. That was the big PHN trial that was published in JAMA.

Q. And Serpell right below that, what did Serpell study?

A. Mixed types of neuropathic pain.

Q. And two more to go. Simpson 2001, that study, it says "Gabapentin and Venlafaxine." What's venlafaxine?

A. It's a serotonin reuptake inhibitor.

Q. And that was also in diabetic neuropathy?

A. Correct.

Q. And then below that is Tai 2002. What type of pain did they study in Tai?

A. Spinal cord injury. And as I had mentioned, damage to the spinal cord and brain can also cause actually very difficult-to-treat neuropathic pain.

Q. What was the conclusion of the Cochrane review after reviewing all these studies?

A. That looking at the literature as a whole, the studies they selected, there is adequate evidence to support that there's efficacy of gabapentin for the treatment of neuropathic pain.

Q. The jury has heard a lot about the Cochrane review. Are the Cochrane reviews reissued from time to time?

A. Actually, they're reissued every five years; and if they're not reissued, and this is one thing that's great about Cochrane, they delete them. So they actually have to be reissued every five years.

Q. Has an update come out recently as well?

A. 2010, it just came out.

Q. The same conclusions?

A. The same conclusions.

Q. Doctor, you also cited several reviews or systematic analyses that found efficacy for gabapentin in decreasing perioperative pain; is that right?

A. Yes.

Q. And those included papers by Gilron, Hurley, McQuay, and Tiippana; is that right?

A. Yes.

MR. HOOPER: Your Honor, I want to move Exhibits 1911, the Gilron review, 1858 is Hurley, 1979 McQuay, and 1933 Tiippana.

(Exhibits 1911, 1858, 1979, and 1933 received in

evidence.)

Q. Doctor, what significance did these papers have to your opinion?

A. It was part of my overall review of the literature. And, frankly, I had heard about the use of gabapentin for the treatment of perioperative or postoperative pain, but prior to that review hadn't done a real in-depth evaluation, and I looked at those references to, you know, learn more about the topic. And, again, what as a group they suggest or find is that there is strong evidence that gabapentin can reduce pain after an operation, typically, as I said, a single dose, which is very interesting, since you wouldn't expect the drug to stay in the system particularly long, certainly not as long as it's providing pain control.

Q. Doctor, let me ask you about some terms we've heard in the case in reference to study results, "positive" and "negative." What do those terms mean to you?

A. Well, I will speak for myself and based -- I think when people use those terms, "positive" usually means there's statistical significance in some form or another, and "negative" means they did not find an effect or effects that they were looking for. But like everything in the world, there is, or I think -- I'm not a black-and-white person -- I think the gray zone is bigger. So studies that might be considered negative, for example, might have a positive outcome in a

secondary measure. And as a scientist, we always say that you can't prove that there's no effect. You can only prove that there is effect. So all these studies are interesting. I don't like the term "negative" because I think even firm studies where there's no statistical significance, there's always something to be learned from them, so I find "negative" to be a pejorative term in this regard.

Q. Can drugs that are in fact effective be studied in clinical trials and produce negative results?

A. Certainly. That happens commonly.

Q. What are some of the reasons that in your experience as a pain specialist, what are some of the reasons that a study could come out negative, even if the drug is in fact effective?

MR. GREENE: Objection, your Honor.

THE COURT: Sustained.

Q. Is it common for pain physicians, for you, is it common for you to have to make decisions as a pain specialist where there's inconsistent information in the literature?

A. Virtually every single patient.

Q. Let's turn to medical decision-making. Doctor, can you explain some of the clinical considerations, doctor and patient considerations that you take into account in making treatment decisions for neuropathic pain patients?

A. Certainly. So we always start with what's called the patient's chief complaint, so what is their pain problem? And

through a careful history and physical exam, we come up with a diagnosis. So really the first line should be the patient's primary diagnosis, their pain diagnosis.

The second is, many of our patients have tried other pain therapies, whether it's medications, injections, physical therapy, et cetera; and you have to know what they've tried to know what hasn't worked, what might have worked well, what might have worked partially. Of course it's critical to know what their other medical problems are. You know, do they have heart disease? Many of the pain patients have depression. So what their other medical problems are, and what are their other medications? Because many of the medications we use interact with other drugs, so those are critical to know. And medications we use, some of them have potentially life-threatening adverse effects that are critically determined by what the patient's other medical problems are. So treating a 21-year-old with sciatica is far different from treating a very ill 90-year-old with sciatica.

Another point is, is the patient going to use the medication as prescribed? And that's a judgment, of course, but, as I said, some of these medications have potentially life-threatening toxicities. So if you don't believe the patient is going to use the medication appropriately -- and there's a broad medical literature to say many patients don't, just because especially if you're on a lot of medications, it's

really hard to take them right -- if you're concerned about that, you're going to tend to give patients medications that are less likely to cause problems if they're used improperly.

And a good example is tricyclic antidepressants which are extremely toxic and will kill virtually everyone who tries to take them in overdose. So if I have a patient with a history of depression and suicidal attempts, I'm probably not going to use a tricyclic in that individual.

And, finally, social history including histories of substance abuse, where they're living, et cetera, because, for example, in a patient with a long history of I.V. drug abuse, I'm probably going to be very -- I'll certainly be very careful about using a controlled substance like a narcotic and probably not use it at all because -- it's not a vindictive thing. I'm here to try to help the patient. If I give them a medication that's going to harm them, even if it might help certain other patients, I haven't done them any good and I haven't cared for them properly.

Q. Doctor, I'd like to turn -- we talked about your clinical practice. Are you familiar with claims in this case about dosing above 1,800?

A. Yes.

Q. I'd like to ask you about your own clinical practice in regard to dosing.

A. Sure.

Q. I'm going to show you Exhibit 507 which is a Neurontin package insert. You cited the package insert in your report, correct?

A. Yes.

Q. Okay. Let me ask you to direct your attention to the "Dosing and Administration" section.

A. Sure. I'm pretty familiar with it, so --

MR. HOOPER: First, Austin, if you could go on the page that has "Dosing and Administration, Postherpetic Neuralgia," blow that up.

Q. Doctor, if you look at the section of the U.S. package insert in the "Dosing and Administration" section under "Postherpetic Neuralgia," do you see there that it says, "In adults with postherpetic neuralgia, Neurontin therapy may be initiated as a single 300-milligram dose on day one, 600 on day two, 900 on day three," and so forth?

A. Yes.

Q. And then the last two sentences I want to call your attention to. It says, "In clinical studies, efficacy was demonstrated over a range of doses from 1,800 milligrams a day to 3,600 milligrams a day with comparable effects across the dose range." And then it says, "Additional benefit of using doses greater than 1,800 milligrams a day was not demonstrated."

What does that mean to you as a practicing physician who

uses this medication?

A. Sure. What that means is, in the trials that the FDA looked at for approval of gabapentin for postherpetic neuralgia, they found that both 1,800 milligrams a day and 3,600 milligrams a day were both effective in controlling the symptoms of the postherpetic neuralgia, but they failed to see a difference between the two doses. And what that means to me is that this was a limited look to some degree at postherpetic neuralgia. Both were effective. It tells me, to be honest, not a great deal. It tells me that those doses in these populations were effective. It doesn't tell me that in another type of neuropathic pain or in any given individual, not populations of individuals, that some people might benefit from 2,700 milligrams versus the 1,800, and it doesn't tell me that I might not have patients who benefit from 900. So, again, this information is very important, but it's based on groups of individuals, not a given individual.

Q. Let me ask you to look lower in that section.

MR. HOOPER: I think it actually spans onto the next page, Austin. There's a table, Table 5.

Q. Doctor, this is still in the "Dosage and Administration" section, Table 5, "Neurontin dosage based on renal function." Can you explain to the jury what this table tells you as a practicing physician?

A. Sure. The first thing --

MR. GREENE: I object. Now we've gone beyond the scope of his report.

MR. HOOPER: He cited the report, your Honor. He's talking about how he prescribes the medication and what the labeling is.

THE COURT: Why don't you talk to him for a minute.

MR. GREENE: Show me where it is.

(Discussion off the record between attorneys.)

Q. Doctor, would you explain what the table --

MR. GREENE: It's not cited within report. It's a reliance material with a one line, your Honor.

THE COURT: Well, I'll allow it.

A. Sure. So the first thing that we have to mention is how this medication is taken out of the body, which is, many, many medications are broken down by the liver. Gabapentin is not. Gabapentin gets into the bloodstream in an unchanged form from the form you take, and the kidney excretes it in the urine, also unchanged, so it's not broken down. So it's very important to know whether the person's kidneys are working properly. If someone's kidney function is really, really down, the drug will build up in their body and can have more adverse effects. So Table 5 tells you how to give this medication to individuals who may have diseases of their kidney which decrease kidney function.

Q. Doctor, looking at the top row of numbers where it says

"Renal function" and it has the number greater than or equal to 60, would that correspond to individuals who have normal or only minimally impaired kidney function?

A. Yes.

Q. And then going to the right, right beside it, it says "Total daily dose range, 900 to 3,600"?

A. Yes.

Q. And then it has a "Dose regimen" off to the right that goes from 300 TID -- is that 300 milligrams three times a day?

A. That's correct.

Q. And then it goes out to 1,200 milligrams three times a day?

A. That's correct.

Q. That would add up to 3,600 milligrams a day?

A. Yes.

Q. And when you see this table and the FDA labeling, what does that tell you about whether doses above 1,800 are on-label or off-label?

A. I think it's a little -- it's internally inconsistent, and I think that, since you're asking me, I think it reflects the fact that there is not absolute understanding about what dose is going to work in a given individual. So as a treating physician, I look at this, and it says to me on one hand the FDA says 1,800 milligrams a day isn't better than 3,600, but on the other hand they're telling me how to get to 3,600. So

they're kind of telling me as a treating physician, there's certainly some patients who you might want to push the dose up higher, presumably because there will be efficacy or better efficacy at the higher doses.

THE COURT: What's up here? Is this the FDA's chart?

MR. HOOPER: That's from the U.S. package insert approved by the FDA for Neurontin, your Honor, yes.

THE COURT: For the postherpetic neuralgia?

MR. HOOPER: Yes.

THE COURT: Is that the label for postherpetic neuralgia?

THE WITNESS: It's the label for gabapentin, which includes postherpetic neuralgia and adjunctive treatment of partial seizure.

Q. And, Doctor --

THE COURT: Yes, did you have a question? Go ahead.

A JUROR: Just a quick question. They give you a range in the package insert that goes from 1,800 to 3,600. Is that an attempt -- again, I'm not sure if this is a correct question or not -- to show you a safe range in which you can operate?

THE WITNESS: I think --

A JUROR: Because, I mean, if the benefits are the same and you have a patient that doesn't respond to 1,800, then you're talking about going upward. Now, they could have put

25,000 there. You know, that would have changed your opinion of how much you could dose somebody?

THE WITNESS: Right, and I think that's also a very good question. Here's something the FDA understands -- and this is really important -- that a tremendous amount of use of medications is off-label. It's legal. They understand it. They understand that there aren't clinical trials for every problem in the world, and there never --

MR. GREENE: Your Honor, we're talking about what the FDA thinks?

THE COURT: Yes, I think this is beyond the scope. So you're just asking what?

A JUROR: In other words, you've got a range there, and it says there's no added benefit within that range from the 1,800 to the 3,600. So if there's no added benefit, again, I would think one of the first conclusions would be, I would give somebody 1,800.

THE COURT: Is that right? Would that be your first approach?

THE WITNESS: I would say that in the very specific indication and not necessarily apply that to all other patients with neuropathic pain, but what I would take away from this is, in the studies that this was based on, and there may be many more that came out since then, and there are that would inform me even more, but based on this label, I would think that if I

didn't get to 1,800 -- let me try to phrase this properly. I wouldn't be able to say it wasn't efficacious in a given individual unless I got to around at least 1,800 because the lower doses might not be within the therapeutic range of the drug.

THE COURT: Okay, thank you.

MR. HOOPER: Just one more question on dosing, your Honor.

Q. Dr. Brenner, in your clinical practice, what are your dosing practices with Neurontin typically in neuropathic pain patients?

A. Sure, and can I ask for clarification? Do you mean in terms of maximum dose or just in general?

Q. In general, including a maximum dose.

A. Well, certainly based on who the patient is, if they're frail, I start at a lower dose and go slower; and if they're more robust, then I can often push the titration faster. But my general philosophy is kind of what I just said, which is, this is how I'll start titrating up. If I see a good effect at a low dose, I may just stop at maybe, who knows? It could be 600 twice a day or 300 three times a day if the effect is that good.

On the other hand, I won't say that I don't have efficacy in this given individual unless I get to -- and it's a little gray zone -- 1,800 to 2,700 milligrams a day. Of course, there

are also patients who never get to that 1,800 or 2,700 because they don't tolerate the side effects, and then I just discontinue the medication.

And one thing I would add, since you asked about my general dosing regimen --

MR. GREENE: Objection, your Honor.

THE COURT: Sustained.

Q. Doctor, in the interest of time, I want to just ask you very briefly about some of the alternative medications that Kaiser has discussed in this case. Had you seen the declaration by a doctor of pharmacy, Dr. Mirta Millares, listing alternatives advocated by Kaiser in lieu of Neurontin?

A. Yes. I believe I actually saw two declarations dated differently.

Q. And did you see on there that among them were the TCAs?

A. Yes.

Q. And another drug for neuropathic pain that they recommended was carbamazepine or Tegretol?

A. Yes.

Q. Okay. Could you discuss just very briefly the relative safety issues as between the TCAs and carbamazepine versus gabapentin.

A. Sure. The bottom line is, gabapentin is globally much, much safer than these medications. So the first thing you have to know is both -- and I'm just going to say Tegretol because

because it's easier to say -- that TCAs or tricyclic antidepressants and Tegretol both have significant toxicities if overdosed, so they both can cause death.

Q. Cardiac side effects?

A. In the tricyclics, mostly cardiac. Tegretol also has significant CNS or brain effects. In fact, you absolutely have to measure blood levels of Tegretol when you're dosing it. Also, they both have cardiac effects. So in patients who have what we call conduction problems or electrical problems in the heart, tricyclics are contraindicated, and I likewise probably wouldn't use Tegretol.

Also, they both have what's called anticholinergic effects, and without getting into detail, it affects some of the neurotransmitter systems in the brain and the rest of the body that can be very limiting. So for the tricyclics, they can cause what's called orthostatic hypotension, which means you're blood pressure goes down when you stand up suddenly, and you can become light-headed. And in an elderly individual -- and this is a real consideration -- they stand up, they get light-headed, they fall down, they break their hip, that can kill someone, or eventually lead to their death.

Q. Do the TCAs and carbamazepine or Tegretol have issues with drug interactions that affect prescribing decisions?

A. Sure, they certainly do, both because they're metabolized by the liver, so they'll be affected by other drugs, so it can

make the levels in the blood go up or down, and they'll also affect other drugs. Also, this anticholinergic component that I talked about, that's additive. So if you have multiple drugs with anticholinergic effect, they work synergistically and can really lead to major problems.

Q. Let's turn to opioids. Did you see in the Millares declarations that Kaiser had listed some medications called "opioids" as alternatives to Neurontin?

A. Yes.

Q. What are opioids?

A. Opioids are the group of drugs that act like morphine. Morphine is derived directly from the poppy plant, as you know probably. There's also partially synthetic and fully synthetic, so you've probably heard of like Percocet that contains an opioid. Dilaudid or hydrocodone, that's an opioid. Fentanyl, all of those are opioids.

Q. Are there potential problems or issues with opioids that affect your prescribing decisions with those medications?

A. There are substantial issues with the opioids.

Q. Can you describe the main ones.

A. Sure. Every individual who receives opioids more than a short period of time is going to develop tolerance. That means the medication doesn't work as well over time. And that's just physiology. Also just physiologic is that every individual will develop dependency, which means if you stop taking them or

decrease the dose suddenly, you're going to have the withdrawal side effects.

There are also significant CNS effects, brain effects. So respiratory depression, if you overdose, there's enough respiratory depression that you can certainly die from overdose due to lack of breathing. They also cause sedation, and, you know, for example, someone who's driving or operating heavy equipment, it can be dangerous. Of course, everyone has heard of addiction, and that's a real risk. About 6 percent of the population, irrespective of your social status or anything like that, has problems with substance abuse, so it's a real problem.

Also diversion, so the opioids have a significant street value. People absolutely sell them, trade them for other things, and they get into hands of people who shouldn't have them. And the last I read, the federal government has estimated that 50 percent of pharmaceutically produced opioids are misused in one form or another.

Q. Doctor, with reference to these issues with the TCAs, carbamazepines, and opioids, the toxicity and overdose, the cardiac side effects, the drug-drug interactions, and these other things you've told us about, how does gabapentin, Neurontin, compare with those medications and -- well, let me ask that.

A. Gabapentin really truly compares very favorably with both,

of those, the Tegretol and the tricyclics as a class, and I'll just briefly go through it. We already talked about the fact that it's not metabolized by the liver, and for anyone who's familiar with this, it's not protein-bound in the blood. Drugs bind to proteins, and it's the part that's not bound that usually is active. So it doesn't bind to proteins and it's not metabolized by the liver, so the bottom line is, it basically doesn't interact meaningfully with other drugs. Very slightly it can cause some sedation, and that can add to the sedation of other drugs, but other than that, there are no drug-drug interactions.

There's no known case, to the best of my knowledge, of death due to either unintentional or intentional overdose. It doesn't have any of those anticholinergenic effects we talked about, so it's really very safe with many different other medical problems, including heart problems. And there's no known addiction potential. So it actually makes Neurontin for us a go-to drug for many patients with neuropathic pain who otherwise either wouldn't tolerate either of those other drugs, or for social reasons, such as a depression or something like that, might try to harm themselves with the other drugs. So it's something we can give a patient and feel very comfortable that the risk we're going to harm them in any meaningful way is negligible.

Q. Doctor, let me change to a different subject before we

conclude very briefly. In Section 10 of your report, you discuss something called ICD-9 codes?

A. Yes.

Q. Okay, what are ICD-9 codes?

A. They're diagnostic codes that are used predominantly for billing purposes. So every time you submit a bill, you have to check off one or often several diagnoses.

Q. Are ICD-9 codes and doctors' use of them something that you're familiar with as a result of your own practice?

A. Yes.

Q. And does your institution use ICD-9 codes regularly?

A. Yes.

Q. Something you encounter on a daily basis?

A. Every time I'm in the clinic.

Q. How useful would those be for matching up prescriptions for a patient with the specific illness that the prescriptions were intended to treat?

A. Overall globally, not very useful.

Q. Why not?

A. For two reasons: The first is, imagine a patient has many medical problems, which many patients do, so they're going to have multiple ICD-9 diagnostic codes. So you take that patient with multiple diagnoses, and you take one medication, and it's impossible to know a priority what -- which of those diagnoses the medication is being used for, if any, because physicians

don't always check off everything, or maybe it's being used for more than one. So in my work, you may have heard of Cymbalta or duloxetine, same drug. It's an antidepressant that's FDA approved for some neuropathic pain types. Sometimes it's used to treat depression and pain in the same person. And secondarily -- or I guess that's cool.

Q. Are there occasions in your practice where you need to look at records and determine what medications a patient who's been referred to you has been prescribed and how they've been treated in the past?

A. Yes.

Q. Is there a method for determining what medications they've taken in the past for what specific indication?

A. Sure. There's two methods.

Q. How would you do that?

A. One is, of course, you always ask the patient, so that's the first method and most important. Secondly is patients will sometimes bring their old medical records, and I will look through the medical records to see what's done and why. But I have to say, that's heavily dependent upon the quality of the documentation. And I've seen this many times, you know, with any medication but including gabapentin, it may say, you know, "Start gabapentin," period, and they don't say why. So basically you have to guess. Sometimes it seems pretty obvious, but sometimes you don't know. And I always for this

reason train my fellows, "Don't just write start X medication. Say initiate trial of X because of Y." But you often don't see that in the medical record, as you guys all know.

MR. HOOPER: Let me bring up Slide 6.

Q. Doctor, in summary, based on your education, training, and experience and the materials you looked at in this case, do you have an opinion on whether Neurontin is effective as a treatment for neuropathic pain?

A. Sure.

Q. What is your opinion?

A. My opinion is that --

MR. GREENE: Objection, your Honor. I think we've been through this.

THE COURT: So, right, this is based on his clinical experience. He's not testifying based on the FDA's standards or the standards for scientific efficacy. It's based on what he's experienced in the pain clinic.

THE WITNESS: That and my understanding of the medical literature.

THE COURT: And the literature.

A. So based on my training, experience with treating patients for ten years, and my reading of the medical literature, gabapentin is very effective for a subset of patients, not every patient but a subset of patients with neuropathic pain. Based on the literature more than my clinical experience, there

also seems to be a signal that it decreases pain after an operation.

Q. And what's your opinion on the safety of gabapentin?

A. As I said, it is a very safe medication, especially in comparison to the alternatives, and it's well tolerated by most individuals. And in individuals who don't tolerate it, we just stop it, and no harm has been done.

Q. How does gabapentin compare with the alternative medications for neuropathic pain, in your opinion?

A. Globally in terms of effectiveness, safety, and tolerability as we've really gone over, I think it's a very important component of our armamentarium of medications for neuropathic pain and compares favorably. And that's not to say I don't use the other medications. Of course I do.

Q. And, Doctor, do you hold each of those opinions to a reasonable degree of scientific certainty?

A. Yes.

MR. HOOPER: Pass the witness.

THE COURT: Why don't we stand up, stretch.

(Pause.)

MR. HOOPER: Your Honor, I need to offer 507. It's the labeling exhibit. I inadvertently left it out, I'm told.

THE COURT: The FDA label.

MR. HOOPER: Yes.

THE COURT: All right.

(Exhibit 507 received in evidence.)

THE COURT: Okay, let's go.

CROSS-EXAMINATION BY MR. GREENE:

Q. Good morning, Doctor.

A. Good morning.

Q. We haven't met before, have we?

A. Not to my recollection.

Q. Do you have a copy of your report in front of you?

A. I do not.

Q. You had the opportunity to listen to Dr. Furberg's testimony last week?

A. No.

Q. Were you in court yesterday listening to any of the testimony?

A. No.

Q. You agree with me that depression can lead to suicide?

A. I would agree --

Q. Just yes or no, do you agree, Doctor?

A. Depression is a risk factor for suicide.

Q. And you know that the FDA in May of 2008 reviewed all eleven antiepileptic drugs and has required a warning to be placed on them regarding suicide, correct?

A. That is correct.

Q. We also had some testimony that you gave the jury concerning dosing. Do you recall that?

A. Today.
Q. Just a few moments ago.
A. Yeah, sure.
Q. Mr. Hooper put the label up for PHN, and you looked at that, correct?
A. That is correct.
Q. And in that label it said that Neurontin had no greater efficacy above 1,800 milligrams? It was the last sentence he highlighted. Do you recall that sentence?
A. It was one of the sentences he highlighted.
Q. Do you recall -- did you know that the FDA in 1993 when they approved Neurontin had looked at five double-blind randomized controlled trials for epilepsy and found no greater efficacy in doses above 1,800?
A. That's my recollection.
Q. You reviewed the Reckless study, didn't you?
A. I reviewed it, yes.
Q. I assume the Pfizer lawyers gave you the protocol and the research reports for Reckless. Did you look at those?
A. I did not.
Q. Did you know that Dr. Reckless found no greater efficacy at a dose of 2,400 than a dose of 1,800?
A. That's my recollection.
Q. Now, I think you told the jury that you're an expert on pain. That's your expertise; is that right?

A. Pain medicine and the science of pain mechanisms.
Q. But you went out of your way to point out that you were not an expert in clinical trials, right?
A. Not exactly.
Q. Well, I think I wrote your words down, "not an expert in clinical trials." Is that what you said?
A. Among other things related to the topic, yes.
Q. Just answer my question. Are you an expert in clinical trials?
A. It depends on how you define expertise, sir.
Q. How do you define expertise?
A. I think, as I said about other topics, the world is not black and white; there's a gray zone. So I went through medical training. I do research on a daily basis. I work on the Institutional Review Board that every time I sit with them we review the ongoing clinical trials. So not to be offensive to anyone, but someone who's never had any exposure whatsoever, do I have more expertise than they do? Absolutely. Are there people around who have much more expertise than me because they focus their entire career on this issue? Certainly. So I have some expertise.
Q. You came into this court to give some opinions regarding whether Neurontin was effective for neuropathic pain, correct?
A. That is correct.
Q. And nociceptive pain, correct? That was one of the

subjects you looked at?
A. I'm not sure I offered an opinion on effectiveness for nociceptive pain. I did as part of the background in my report discuss nociceptive pain to broadly educate about the different forms of pain, which really aren't generally appreciated.
Q. Okay. Your report is 13 1/2 pages, isn't it?
A. I'll take your word for that.
Q. Well, you have it right in front of you if you want to look at it.
A. I'll trust you on numbers.
Q. You said you reviewed Dr. Perry's report, correct?
A. I did.
Q. And that's his report, 80 something pages, correct?
A. I'll take your word for the number there.
Q. And the appendices to his report that he put together exceed 300 pages, correct?
A. I'll again take your word for it.
Q. Well, did you review Dr. Perry's appendices?
A. I did look through them, yes.
Q. Dr. Perry performed a meta-analysis of all the double-blind randomized controlled trials that studied Neurontin in treating neuropathic pain and nociceptive pain, didn't he?
A. He did review quite a few. I'm not sure "all" is an appropriate way to describe what he did.

Q. Well, let's look at Page 4 of your report. Did you write there at the top of the report, the paragraph that begins with "Due to the large number of studies of gabapentin and neuropathic pain, it would be extremely cumbersome to address the primary medical literature in its entirety"? Is that what you wrote?

A. I did.

Q. You didn't undertake a review of all of the defendants' studies, the protocols and the research reports, correct?

A. In terms of what, sir?

Q. Did you look at the actual research reports for Neurontin studying neuropathic pain and nociceptive pain?

A. I didn't look at all of the full protocols, complete protocols and data sets --

Q. That's all I'm asking you. Did you look at that data?

A. I did look at the data.

Q. These lawyers actually gave you the research reports, the protocols, and you reviewed all of them?

A. It was embedded in several of the plaintiffs' expert testimony, written testimony, and I read it in the plaintiffs' reports.

THE COURT: So which experts did you read?

THE WITNESS: I think that's in my report here actually. If it's not -- frankly, it's a pretty long list, but it includes Abramson, obviously Perry, Dickersin, a variety of

experts on efficacy, a variety of experts on suicidality and anticonvulsants, but, yeah, on Page 17 in the appendix, Section 6, "Materials Reviewed."

Q. Well, I'm looking at Page 18, No. 14, "Pfizer-sponsored studies related to gabapentin," and you list five of them there. The first one is POPP. The next one is one of the nociceptive studies. Actually the next three are, and the last one is Reckless.

So those five that you listed in your report, what I'm asking you is, like Dr. Perry, did you take the defendants' protocols and the research reports and go through them and read them from cover to cover? Yes or no.

A. Cover to cover? No.

Q. What you did is, you turned to the Cochrane Collaborative, correct?

A. It --

Q. Didn't you look at the Cochrane Collaborative review?

A. That was one of the components of the medical literature I relied upon, yes.

MR. GREENE: Could we have that exhibit, please, 1772.

Q. While we're pulling that up, in your report you said that the Cochrane Collaboration is one of the most respected groups performing meta-analysis reviews; is that right?

A. I did write that.

Q. And that's why you say you turned to them, correct?

A. That's why I included this meta-analysis as part of my review.

Q. Well, you didn't do your own meta-analysis as Dr. Perry did, but you turned to the Cochrane Collaborative meta-analysis, correct?

A. I did not perform a meta-analysis, no.

Q. And you reviewed Dr. Perry's report. You know he did, correct?

A. I read his report in its entirety.

Q. Well, if you read his report in its entirety, you know that he conducted a meta-analysis because the Cochrane review was incomplete, correct?

A. No.

Q. You looked at the Cochrane review, right? We just reviewed it with the jury. Is that right?

A. Yes.

Q. And that was the 2005, correct?

A. Yes. That just -- that wasn't why he reviewed it. I'm answering your question, sir.

Q. Did you look at the 2005 Cochrane review?

A. Yes.

Q. And we recited the references there, didn't we?

A. Can you repeat that, please.

Q. You recited the references to the Cochrane review?

A. Yeah, I responded to --

Q. And nowhere there was Dr. Reckless' study listed, correct?
A. That's correct.
Q. And nowhere there was the POPP study listed, correct?
A. That's correct.
Q. Dr. Reckless' study was the largest clinical trial that the defendants had undertaken to study Neurontin's use in treating diabetic peripheral neuropathy, correct?
A. That's my understanding.
Q. So tell the jury, when did you know that the Cochrane review lacked those two double-blind randomized controlled trials?
A. At the time that I read it.
Q. At the time you read it. So you knew it was incomplete because it lacked that data, correct?
A. I wouldn't describe it as incomplete. I would -- you know, the authors of the review, in fact from 2010, are aware of those other data and specifically write that they chose not to include them.
Q. Doctor --
A. And this is how meta-analysis works, which is the authors of the meta-analysis exclude --
Q. Doctor, can you try to answer my question, please. We're going to get to the 2009 Cochrane review.
A. Sorry, 2010.
Q. Right now we're talking about the 2005 Cochrane review,

the one we have up.
A. Okay.
Q. You say that you were aware that it lacked the POPP study and the Reckless study. Did you mention that in your report?
A. No.
Q. If the jury wanted to find what you thought of the Reckless study, where would they find it in the 13 pages of your report? Where is it specifically discussed?
A. In the overall conclusion. It's in my report that I reviewed it, and it's part of what I considered.
Q. Show me your discussion in your report of Dr. Reckless' negative study.
A. There is no specific discussion.
Q. All right, thank you. Show me in your report your discussion of the negative POPP study.
A. The same answer.
Q. It's not there, right?
A. There's no specific discussion.
Q. So you chose to rely on an incomplete Cochrane summary, and when you did it, you knew it was incomplete?
THE COURT: Compound question.
MR. HOOPER: Objection.
THE COURT: Two questions. You need to ask one.
THE WITNESS: Should I answer the first question?
MR. GREENE: Let me rephrase it, Doctor.

THE COURT: Let him rephrase it.

Q. You relied on a Cochrane 2005 study that lacked the POPP study and the Reckless study? Yes or no.

A. I relied in part upon it, yes.

MR. GREENE: Go on to Exhibit 2046.

Q. Do you have that up on the screen? Now, this is the study that I referred to as the Cochrane 2009, and you pointed out it's 2010, correct?

A. It came out in 2010.

Q. I don't think you put this up on the screen with Mr. Hooper, did you?

A. I don't put anything up on the screen, but I think --

Q. Right, Mr. Hooper just asked you, was the 2010 Cochrane study the same, and you said "yes"?

A. I didn't say "yes." I said their conclusions.

Q. Well, let's look at it. Let's turn to the abstract, the very first sentence on background, February, 2009. Do you have it in front of you? Just follow along with me, Doctor. "February, 2009: The authors are aware of unpublished trial data for gabapentin which could affect the results of this review. This information together with that from trials published since 2005 will be considered when this review is updated in 2009."

Did you put that in your report?

A. That information --

Q. Did you put it in your report? Yes or no.
A. It wasn't available at the time.
Q. The POPP study, you knew the POPP study hadn't been published, correct?
A. I was aware of the POPP study.
Q. Right. That's unpublished data they're referring to there in 2009, correct?
A. I'm not sure specifically which unpublished data they're referring to.
Q. Well, you knew the Reckless study was negative and hadn't been included, right?
A. I was aware that they hadn't included the Reckless study.
Q. Let's turn to Page 4 of the abstract, highlighting the last sentence under "Results."
"Gabapentin currently has no role in the management of acute pain, as more effective analgesics are available."
Did you put that in your report, Doctor?
A. I didn't discuss acute pain in my report.
Q. The next page under acute pain, "There is no logic in using anticonvulsants to manage acute nociceptive pain." Did you put that in your report?
A. No, and I believe I testified earlier that I agree with that at this point, at least for gabapentin.
Q. You talked a little bit about ICD-9 codes. Did Pfizer give you any ICD-9 codes to put in your report?

A. Pfizer?
Q. Yes, Pfizer.
A. You mean the attorneys who --
Q. Yes.
A. I reviewed ICD-9 codes associated with --
Q. No, no, my question is did Pfizer, did the company Pfizer give you any ICD-9 codes to put in your report?
A. I'm sorry, I don't -- I kind of don't understand the question.

MR. GREENE: That's all I have, your Honor.

MR. HOOPER: Just one question, a couple questions, your Honor.

REDIRECT EXAMINATION BY MR. HOOPER:

Q. The Cochrane review that you just talked about, after they put the insert in in 2009 that said they were aware of unpublished data that might change the conclusion, was reissued earlier this year, wasn't it?
A. Correct.
Q. About three weeks ago, wasn't it?
A. Correct.
Q. What were the results?
A. They didn't change --

MR. GREENE: Objection, your Honor.

THE COURT: Sustained.

MR. HOOPER: That's all, your Honor.

THE COURT: Thank you.

THE WITNESS: Thank you, your Honor.

(Witness excused.)

THE COURT: What are we doing now, the depositions?

MR. CHEFFO: Yes, your Honor. We can do them right now, or we can take a few minutes to set up, whatever you --

THE COURT: How long will it take to set up?

MR. CHEFFO: We do need to finish Dr. Glanzman.

THE COURT: Yes, let's finish Dr. Glanzman's deposition. Do you have that ready?

So we've been trying to get the doctors on and off the stand. So we're going to go back. You might even want to rewind like a couple of minutes to put us back in context. This is Dr. Glanzman from Pfizer, the -- is it director of -- who's he now? The director of medical --

MR. GREENE: He's a medical doctor, Pfizer's medical doctor that sits on the Neurontin Publication Committee that works with MAC and --

THE COURT: All right, so I don't remember where, it's been so many days now that we broke off. Did you rewind it just a little bit so we can just remember? And how much longer did we have? Do you remember? Maybe we'll do ten minutes.

MR. GREENE: I think it was less than ten minutes, your Honor.

THE COURT: All right, ten minutes. Then we'll take

our morning break. Then they'll get set up. They have a round of depositions too. I think he's the last live witness today, right?

MR. CHEFFO: That's correct, your Honor.

THE COURT: Yes, okay, let's go.

(Video deposition played of Robert Glanzman, M.D.)

THE COURT: Oh, less than ten minutes. All right, thank you. Well, before we do, and? Do you rest?

MS. NUSSBAUM: Subject to a side bar on three documents, your Honor.

THE COURT: All right, so subject to three documents which we'll resolve, do you rest?

MS. NUSSBAUM: Yes, your Honor.

MR. GREENE: And subject to what we said the other day concerning the exhibits that you're reviewing, the binders.

THE COURT: Yes, subject to some documents that are still in dispute, do you rest?

MR. GREENE: We do, your Honor.

MS. NUSSBAUM: Yes, your Honor.

THE COURT: All right. That had been delayed simply because we were trying to accommodate these other doctors' schedules. Okay, I'll see you about 11:15.

THE CLERK: All rise for the jury.

(Jury excused.)

(A recess was taken, 10:45 a.m.)

SIDE-BAR CONFERENCE:

THE COURT: Why don't you just preserve it.

MR. CHEFFO: Just for the record, since they've now rested, we move formally pursuant to Rule 50 and incorporate by reference all the grounds that we had articulated in our motions which were filed yesterday and shared with counsel.

THE COURT: Yes, okay, so I haven't ruled on that yet. The plaintiffs have said they want to respond to it, which they'll do Thursday by 5:00, let's say. We will have at least some oral argument on it on Friday, and it's preserved.

Now, on the documents, as I mentioned, I thought I had resolved, but I didn't check to make sure every single document was referenced in the memo written by Mr. Sobol; but unless someone tells me otherwise, if it's referenced, they were all quoted and I saw the relevance of them, so I'm going to allow them in. But I didn't know about three other documents.

MS. NUSSBAUM: We gave them -- I gave them yesterday morning to Mr. Fox. He was going to review them and get back to me. I asked him again this morning. Somehow it had fallen between the cracks, so hopefully by the end of this break he'll get back to me and we'll know the answer.

MR. CHEFFO: Let me say, I think that from our perspective, your Honor, these are documents your Honor ruled on already. Basically for some of the things, they talk about Lipitor, they talk about GM's plant. You had ruled earlier on

that if it talks about Kaiser or it talks about Neurontin, it comes in. These are thick documents that they're now trying to, in our view, reargue --

THE COURT: And that's precisely it with respect to the all the documents that relate primarily to the enterprise. I mean, that's what the documents were in the binders that Mr. Sobol wrote the brief about. If there are other parts that you want to move to strike and sanitize, I'd be open to that; but I'm allowing in the documents at least with respect to the quotes that were in the memo and the context.

MS. NUSSBAUM: With due respect to Mr. Cheffo, the three documents --

THE COURT: I can't rule --

MS. NUSSBAUM: No, no, no -- they were with the first witness, Mr. Carrejo, and at that time we said we would have a side bar. Then we've all been very busy. We never had the side bar.

THE COURT: Okay, so you'll discuss it.

MS. NUSSBAUM: Since then things have gotten looser. Whole documents are going in. And so we gave him these three documents yesterday, and, you know, if we can reach an accommodation, that would be great.

THE COURT: Why don't you go discuss it during the break it, and I'll worry about it. It at least goes in with respect to the part that Mr. Carrejo testified about. And,

yes, you're right, sometimes people objected to the whole document and sometimes they haven't. I've definitely said, with respect to the three binders Mr. Sobol gave me, that I was allowing them in with respect to the quotes that he was relying on. I'm giving them the option, if there are parts that are completely irrelevant and want to be sanitized, I leave it up to them to move to strike it. So similarly here, you need to talk and go through them.

MS. NUSSBAUM: That's what I wanted to do. We gave them to them yesterday. We'll go through them.

MR. CHEFFO: I mean, this is the point --

MS. NUSSBAUM: Let's talk about them, Mark. I've asked you three times. Let's talk about --

THE COURT: Go talk. That's fine. Perfect.

MR. FOX: And, your Honor, just one other thing. We had also offered yesterday into evidence under Rule 106 a binder in connection with plaintiffs' proffer of their binder No. 3.

MR. CHEFFO: For completeness, I think your Honor had ruled that we can put that in?

MS. NUSSBAUM: Have you seen that? Yes, we haven't --

MR. FOX: Mr. Sobol has.

MR. GREENE: I haven't had an opportunity to talk to him, and he is not here.

MS. NUSSBAUM: Well, you know what, I'd rather talk to

Mr. Sobol, who was in real pain and had to leave, so we will talk to Mr. Sobol and get back to you.

MR. CHEFFO: Well, I think, your Honor --

THE COURT: Excuse me, I'm trying to find -- I'm just at this point overwhelmed. What is the thing I was supposed to still rule on you? Oh, it's the deposition of --

MR. CHEFFO: McCarberg.

MR. FOX: McCarberg, right.

MR. CHEFFO: It's pretty short, your Honor.

MR. FOX: And we highlighted the things that we thought consistent with your rulings of --

THE COURT: Fine, so I'll try and do that over the break, but I don't know now what you're talking about.

MR. FOX: Well, yesterday we had given the plaintiffs a list of documents that we thought under the rule of completeness should be included with their Binder 3.

THE COURT: Sure.

MR. FOX: And so we offered them -- we had sent them a list of these documents the week before, and I gave a binder of it to Mr. Sobol yesterday when we offered it.

MR. CHEFFO: I thought your Honor ruled on it.

THE COURT: No, excuse me, excuse me. I made Sobol go through the exercise of giving me the quotes from every document that he thought was relevant primarily to the enterprise theory, and he did that. And so if you similarly

show me why they're relevant, I'm happy to do this, you know?

MR. GREENE: I haven't seen this binder yet.

THE COURT: Yes, so you'll spend some time on it.

MS. NUSSBAUM: He'll give the memo. He'll give as the Judge just said the same thing we did --

THE COURT: Yes, it's not a biggy. We still have a few days here. When are we going to the jury?

MS. NUSSBAUM: Tuesday, Wednesday?

MR. CHEFFO: Well, it depends on what your Honor is contemplating with respect to a conference with us and when you're going to charge. I mean, I think timingwise, again, back to the envelope, probably we'll finish Monday because we'll run out of time by then. So if your Honor was --

THE COURT: I'd like to tell the jury that and give them some hope.

MR. CHEFFO: How are you planning on dealing with it on, like, let's say just timing? Because if you're going to give both sides two hours each, that's four hours. I think you said it's going to take about an hour to charge. Just from a logistics perspective, what is your thinking on --

THE COURT: Well, we'll have to go all day. I would think we would go -- we can do this off the record. Lee's tired.

(Discussion off the record.)

(End of side-bar conference.)

(A recess was taken, 10:53 a.m.)

(Resumed, 11:30 a.m.)

THE COURT: Who is plaintiff's counsel that objected to the McCarberg deposition?

About 90 percent of it was just frivolous. Just frivolous. I spent my entire afternoon yesterday doing this. I was reading your briefs until 11:00, and for me to have to give up my break to do the objections on the McCarberg is insane. There were a couple that I sustained. Like you objected to every single question, and I just think it's getting more contentious and not less contentious. You're objecting to everything. You're objecting to everything. It's not really being worked out.

So are there anymore of these? Because I'm not doing it until you've consulted.

MR. CHEFFO: That's it, your Honor.

THE COURT: You've essentially destroyed every break I've had and every evening with things that could be worked out.

So here it is.

So let's bring the jury in.

(Jury entered the courtroom.)

THE COURT: We're going to play the -- aren't you going to play it?

MR. CHEFFO: We're going to play the video, your

Honor, I'm just going to explain in two sentences who Dr. Maizels is, your Honor.

THE COURT: Let me just say this.

You're going to hear depositions of a bunch of doctors. Most of them are not from Kaiser or Kaiser Permanente. You've heard this. This is part of a big multidistrict litigation. That's why it's here. They consolidated all the cases in this district. So some of these doctors represented other people, if I'm understanding it correctly, and the other people -- their depositions were taken, right?

MR. CHEFFO: There's actually, I think, a total of six doctors, four were Kaiser Permanente doctors, two are not. The two we're going to hear from today are from Kaiser Permanente.

THE COURT: So they are being allowed to testify as to their practice, not as experts. They're not the people who did the clinical trials, they're not the people who -- they are practicing doctors and how they go about their prescribing practices. That's what they -- not dissimilar from some of the other folks that you've just heard. Why did they prescribe Neurontin or what limitations did they put on the prescriptions of Neurontin.

Sometimes they are referring to what they heard from another doctor, maybe another -- I don't remember exactly, a psychiatrist or another neurologist or something like that.

That's all hearsay, but I'm allowing some of it only for the state of mind of the doctor, why he prescribed something. Because when you go back to that jury room, you're going to be asked a lot of questions, and one of them has to do with, was there a fraud? Was there -- you'll hear all of it -- and part of it is causation. And so you're going to -- did -- why were these doctors prescribing this stuff?

So I'm allowing in the hearsay not because it's true, what the other psychiatrist said or what the other neurologist said, but what was the doctor thinking when he prescribed something. So you understand how the practice works.

And was there a third thing I was going to say?

Was there anything else I was going to say?

MS. NUSSBAUM: No.

THE COURT: Remember when you parse it through, only some of these are from Kaiser Permanente, some are not, you'll have to parse it for that.

MR. CHEFFO: Can I just tell the jury who Dr. Maizels is, who they're going to hear from?

THE COURT: Isn't it in the deposition?

MS. NUSSBAUM: It is, your Honor, and he's also a former PMG physician.

MR. CHEFFO: I was just going, as Mr. Greene did, give a two-sentence introduction.

THE COURT: Yeah.

MR. CHEFFO: Basically, Dr. Maizels is -- he had been with the Southern Permanente Medical Group since 1993, a headache specialist, and a member of the Department of Family Practice at Kaiser Permanente Woodland Hills facility.

THE COURT: Where's Woodland Hills facility?

MS. NUSSBAUM: California.

MR. CHEFFO: Somewhere in California, your Honor.

THE COURT: North or south?

MR. CHEFFO: Southern California.

MS. NUSSBAUM: But he is a former employee.

THE COURT: Former employee.

MR. CHEFFO: As of this year, I think.

(Played deposition of Morris Maizels.)

MR. CHEFFO: Your Honor, at this point we would just move admission of Exhibit 788, which is this article.

THE COURT: All right.

(Exhibit 788 received into evidence.)

(Played deposition of Morris Maizels.)

THE COURT: So there's a problem here.

MR. CHEFFO: I think that was the court reporter reading the question back, your Honor.

AUSTIN: I'll play it back.

(End of videotape.)

THE COURT: Who is the next doctor?

MR. CHEFFO: Next doctor, your Honor, is Dr. Chandler.

And this is short, it's just about 12 minutes.

THE COURT: Who's he?

MR. CHEFFO: Dr. Chandler is a general psychiatrist who's practiced at Kaiser, again, Southern California Medical Group since 1979, and he's board certified in psychiatry.

And this was October 30, 2007.

(Played videotape of David Chandler.)

MR. CHEFFO: Your Honor, we'd offer Exhibit 653, which is a Kaiser e-mail.

THE COURT: All right.

(Exhibit 653 received into evidence.)

(End of videotape.)

MR. CHEFFO: Your Honor, the next --

THE COURT: Can I just say one thing here? That would be a classic example of someone who talked a bit about other psychiatrists he may have talked with or his understanding of how gabapentin worked. He's not an expert in how gabapentin works. Some of that was hearsay. That was a lot of what his state of mind was for those individuals he did for prescribe Neurontin for.

For that limited purpose only, not for the truth of the matters asserted. But I wanted to flag that, that would be a good example where that might come in in one of the doctors.

Go ahead.

MR. CHEFFO: And Dr. Robin Dea is another Kaiser

Permanente psychiatrist. She's practiced with the Northern California Medical Group since 1979. She was board certified in psychiatry in 1983, and this was taken on September 28th of 2007. This is about 13 minutes, your Honor.

(Played videotape deposition of Dr. Robin Dea.)

(End of videotape.)

MR. CHEFFO: We have the last one, your Honor, it's Dr. William McCarberg. He joined Southern California Permamente Medical Group as a full-time physician in 1982. He's certified in geriatrics by the American Board of Pain Medicine. And this one was taken on September 27, 2007.

This is about 20 minutes, so it may take us just a few minutes over the end.

(Played deposition of Bill Harold McCarberg.)

MR. CHEFFO: Your Honor, I move Dr. McCarberg's article, which is Pfizer 795.

THE COURT: All right.

(Exhibit 795 received into evidence.)

(Played deposition of Bill Harold McCarberg.)

THE COURT: How much longer?

MR. CHEFFO: I think two or three minutes.

THE COURT: Do you want to finish?

AUSTIN: About five minutes.

THE COURT: Why don't we just break then, because you have more depositions.

MR. CHEFFO: We do. We have to continue on Friday anyway, your Honor. That's fine if we break.

THE COURT: All right. Now, let me just give you a sense of where I think this case is going. Obviously, tomorrow and the next day are off because I'm in New Orleans. Then on Friday, a full day of Court, 9:00 to 1:00.

The case should be going to you, as the jury, Monday, Tuesday, or Wednesday, and I'm not sure exactly which day that is yet. So in planning your schedule, if I were to predict right now, I would predict that we will have closing arguments on Tuesday and instructions of law, we will go a full day to get it to you, and then my guess is you'll be exhausted at the end of the day and you'll probably go into the next day, at least, deliberating, which brings us into Wednesday.

Now, there's an off chance, Murphy's law, someone gets sick, we have a snowstorm, another Noah's flood, something, it could go Wednesday. There's also a chance it could finish early and we could at least start the closing arguments on Monday. But if I were a betting person, Tuesday would be the day.

So I would just make sure your schedules are adjusted appropriately for next week. We're going to have a chance, I think, to talk about some of the issues with the lawyers during the afternoons, I'll be doing charge conferences and the like. There's no way this will go to you until Monday. So that's the

general timing on the whole thing.

You've got some homework to do, to read those transcripts, and then we'll see you all on Friday.

Thank you.

THE CLERK: All rise for the jury.

(Jury left the courtroom.)

(Discussion off the record.)

MR. CHEFFO: The only issue I have, you can't have a slide with the "X" through it.

MR. GREENE: We're not.

MR. CHEFFO: As long as it was shown --

THE COURT: I guarantee you none of this is going to make or break this trial. She's going to be mesmerized by Gibbons. Late at night. Some statistician and inspiration from him.

MR. GREENE: Before you leave --

THE COURT: Right now.

(At sidebar on the record.)

THE COURT: I've given you each a draft special verdict form, which is literally a draft. I thought it would be useful to have because it's the way I'm thinking about the case right now and the kind of questions -- it's very complex. Maybe some of it will go away on a directed verdict, but it's how I'm currently thinking about it. And the area that I particularly would like some help on is statute of limitations,

whether I really need all of those questions. It's very hard to frame them because there are so many indications is the big issue that I'm having.

Second thing is I'm about to bring down a draft set of jury instructions that we've been working on. I am not satisfied with the California unfair practices one in particular. I'm just struggling with how to tell a jury about it. I'm just struggling with it. How do you say what fraud is? They say it's not common law fraud, so then what is it? They say it's not -- I'm having trouble with it, and apparently, according to my law clerk who has been struggling with it, too, different panels say different things about it.

So maybe that's -- maybe that's just the nature of the beast. I can't answer that, but I will give you a draft of what we've got so far, but very much to understand it's a work in progress. But I thought we could start the charge conference on Friday afternoon, interlaced -- particularly I'm interested in understanding whether I need all these questions on statute of limitations, which would make this almost an unbearable form, as you can well imagine.

MR. CHEFFO: So you have a draft of the statute of limitations, we'll take that --

THE COURT: No. You have a draft of the verdict form there, my law clerk should be coming down with a copy of the --

MR. CHEFFO: The statute?

THE COURT: -- a draft charge.

MR. CHEFFO: And we can give you comments on Friday.

THE COURT: Absolutely. I thought I would start the process with what I call a raw draft. I was hoping to work on it a little over the break but did not do so.

I don't even understand why someone objected to 90 percent of the questions in there unless it was just more of a catch-all objection, which would have been useful because it just took so much of my time to get through.

But, in any event, that's where we're at. And then we can go off the record on Shearer.

MR. CHEFFO: Yes.

(Discussion off the record.)

MR. GREENE: I just want to go back on the record on the order of witnesses. I understand that Friday we're going to have Bird and Slaby. Is that it, or who else?

MR. CHEFFO: You need to tell me, then, how long your crosses are going to be.

MR. GREENE: I told you. You asked me that, I said I'm trying to keep them short, maybe a half an hour each, might go over a little bit, might go under a little bit.

MR. CHEFFO: As I've told you, we're going to have probably a half hour for the read depositions, there's no video.

THE COURT: No, no, skip the depositions, we'll put

those off, we'll get rid of the live witnesses first.

MR. CHEFFO: Okay. Actually, I think, your Honor -- we'll do whatever you want, it might make sense to do it, we can talk about it, the timing, because we have Bird definitely on and off, first thing, no problem. Then we're going to put Slaby on. The only issue then will be --

THE COURT: Keeley.

MR. CHEFFO: If Keeley can only come for 20 minutes at the end, we think it might make more sense to read the videos and then have him on and off Monday.

THE COURT: I'm completely fine with that. If Keeley came, we would defer the videos.

MR. CHEFFO: Understood, it may make more sense.

MR. GREENE: Just so I know, Mr. Sobol is doing him. I got to know --

MR. CHEFFO: Is doing who?

MR. GREENE: Keeley. Is he coming Friday or Monday?

MR. CHEFFO: I just said that.

THE COURT: When will you know?

MR. CHEFFO: I will definitely know if you tell me more definitely. I think we'll know this afternoon if we can get together on timing.

MR. GREENE: Judge, I'll say it again a second time on the record.

When you say "timing," I'm telling you approximately

30 minutes each.

MR. CHEFFO: Do you want to take the Judge's time to look at the clock?

THE COURT: Thirty minutes each is what he's saying. Is there going to be any Kaiser person coming in on Monday?

MS. NUSSBAUM: Pfizer.

MR. CHEFFO: No, I don't anticipate any Pfizer witnesses.

THE COURT: So you can allocate -- you've used everything up and someone shows up. That is not going to happen.

MR. GREENE: So Arrowsmith-Lowe --

THE COURT: I don't need to be here.

MR. CHEFFO: Arrowsmith-Lowe is not Friday. I just said that three times.

THE COURT: That's what we're doing. We're coming down. We should have -- my law clerk's probably -- if one of you can at least stick around.

The one last thing is if you can have someone, if you're not all going home, start going through the exhibits. I think there is an off chance we could finish this on Monday.

MR. CHEFFO: I agree. I'm anticipating Monday.

THE COURT: I'm saying we could start oral arguments on Monday. We'll know Friday.

MR. CHEFFO: Possibly. It's up to you.

THE COURT: How cool would that be?

MR. CHEFFO: I don't know if we'd be able to finish oral arguments, if you want to go over on them. I'll let your Honor decide.

THE COURT: I'm ready, as you can tell.

(Discussion off the record.)

MR. KENNEDY: Your Honor, do you pre-instruct before and after?

THE COURT: You know, great question. In this case I was actually thinking of it. So think about whether you like that idea when you see this verdict slip, see how I'm thinking of it. Think about that, whether you want -- not usually, but this might be a beautiful example of when it would be appropriate.

MR. KENNEDY: Thank you.

THE COURT: Good idea.

MR. CHEFFO: Thank you, your Honor.

(Court adjourned at 1:15 p.m.)

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CERTIFICATION

We certify that the foregoing is a correct transcript of the record of proceedings in the above-entitled matter to the best of our skill and ability.

/s/Debra M. Joyce — March 16, 2020
Debra M. Joyce, RMR, CRR — Date
Official Court Reporter

/s/Lee A. Marzilli — March 16, 2010
Lee A. Marzilli, RPR, CRR — Date
Official Court Reporter